REMARKS

Applicants request favorable reconsideration and allowance of the subject application in view of the preceding amendments and the following remarks.

Claims 1, 4-29 and 32-33 are pending in the application, with claims 2-3, 30 and 31 being withdrawn from consideration. Claims 1, 7, 13, 24, 28 and 29 have been amended.

Claims 2-3, 30 and 31 have been cancelled without prejudice or disclaimer, thus rendering moot the Examiner's objections and rejections to these claims.

Claims 1 and 13 are independent. Claims 1 and 13 have been amended to include the subject matter of claim 2 and recite the specific regulatory regions for use in the present invention. Claims 1, 13, and 24 have been amended to recite specific genes of interest. Claim 28 depends from claims 25, 24 and claim 1 - the proteins listed in the earlier claims made the list in this claim redundant. Claim 10 is not amended in the present response. Claim 13 has been amended to recite the specific promoters and genes of interest as indicated above. Claim 24 has been amended to further recite selections of the genes of interest - support as indicated above. Claims 28 and 29 have been amended to remove the listed proteins as they are already listed in amended claims 1 and 24 from which these claims depend. Claim 14 depends from claim 6 and ultimately from claim 1. The Examiner acknowledges that there is support for producing beta-glucosidase, endoglucanase II, beta-mannanase, laccase I, and xylanase (See Office Action at page 4, middle of 2nd full para.). These proteins, except for xylanase, now are listed in amended claim 1. Claim 6 depends from claim 1, and includes the limitations of the parent claim.

The promoters now recited in claim 1 and 13 were previously recited in dependent claim 2. They are also disclosed in page 12, 2nd paragraph. The genes of interest that are recited

in the groups of claim 1 and 13, as well as the proteins listed in claim 24, have support in the specification, for example at page 14, last line to page 15, line 2; they are also specified in the specification examples discussed in more detail, hereinafter. Support for the genes of interest recited in these claims also may be found throughout the application, for example on page 14, last line to line 2 of page 15, pages 33-36 (Tables 2 and 3; Examples 12 and 13), pages 47-49 (Table 9; Example 25), pages 51-53 (Tables 10 and 11; Example 29), pages 57-58 (Example 33).

Double Patenting Rejection

Claims 1-21 and 24-33 have been rejected under the doctrine of obviousness-type double patenting as Examiner alleges that the claims are unpatentable over claims 1-29 of Applicant's U.S. Patent No. 6,015,703. Applicant submits herewith a Terminal Disclaimer. Applicant therefore requests the withdrawal of Examiner's double patenting rejection.

Rejection under 35 U.S.C. §101

Examiner rejected claims 1-33 under 35 USC 101, alleging that the claims are directed to non-statutory subject matter because they do not particularly point out any non-naturally occurring features. Applicant respectfully disagrees with Examiner.

Claims 2-3, 30 and 31 have been cancelled without prejudice or disclaimer, thus rendering moot the Examiner's objection to these claims on statutory subject matter grounds

Applicant submits that claims 1, 4-29, 32 and 33 of the present invention are not directed to naturally occurring products. For example, claim 1 defines the nucleotide sequence:

1) a regulatory region selected from *cbh1, cbh2, eg1, eg2, eg3, eg5, xln1,* or *xln2*;

2) a xylanase secretion sequence; and

3) a gene of interest encoding a protein selected from the group consisting of a mananase, a laccase, an endoglucanase, and a cellobiohydrolase.

As can be readily determined, each of these combination of elements that make up the nucleotide sequence defined in Claim 1 are not naturally occurring, and rather require the hand of man for their creation. For example, the combination of a xylanase secretion signal and a mannanase, laccase, endoglucanse or cellobiohydrolase does not occur in nature. A similar limitation is present in claim 13. As claims 4-12, 14, 24-29, 32 and 33 depend ultimately from claim1, and claims 15- 23 depend ultimately from claim 13, these claims include the limitations of the independent claims. As a result, it is submitted that the term "isolated" or "purified" is not required within the present set of claims, and removal of the rejection of claims 1-33 under 35 USC 101 as being directed to non-statutory subject matter is requested.

Written Description under 35 U.S.C. §112

Claims 1-33 have been rejected under 35 USC §112 first paragraph, for failing to comply with the written description requirement. Applicant respectfully disagrees with Examiners position.

Applicant submits that sufficient support has been provided to demonstrate enhanced expression of a gene of interest when fused to a xylanase secretion signal to satisfy the requirement for a broad, genus-type claim. Reference is made to Examples 12-18 (page 33-41; enhanced β-glucosidase expression), 25, (page 47-49; enhanced endoglucanase expression), 29

(pages 51-53; enhanced mannanase expression), 31 (pages 55-56; enhanced high pH endoglucanase expression), 33 (pages 57-58; enhanced laccase expression), and 38 (pages 61-62; enhanced xylanase expression). These, and related, examples describe the source of the genes of interest, secretion signal, and regulatory regions used for the preparation of constructs. These examples also describe the transformation and assay protocols, and provide results that demonstrate enhanced expression of a gene of interest in the presence of the xylanase secretion signal. Furthermore, it is submitted that these examples provide sufficient evidence that many different genes of interest exhibit enhanced expression using the nucleotide sequences, vectors, and methods as claimed, and that these example demonstrate possession of the invention in a broad manner.

Furthermore, the Examiner appears to suggest that a listing of various specific nucleotide sequences are required for each of the described vectors, in order to satisfy the written description requirement. Applicant respectfully disagrees. The examples provided in the specification provide ample written description of the claimed invention. The sequences of the genes of interest that have been disclosed as useful within those examples are known within the prior art. Modifications to these sequences, and information to construct the nucleotide sequences of the present invention are provided in the specification. For example:

- the cloning of cellobiohydrolase and β-glucosidase is described in Example 3 (pages 22-24), and the construction of expression vectors is described in Examples 5-7 (pages 27-30);

- the cloning of xylanase is described in Example 4 (pages 24-26) and construction of expression vectors is described in Examples 34 (page 58-59) and 38 (page 61);

- cloning of endoglucanse is described in Example 23 (pages 44-46) and the

construction of expression vectors is disclosed in Example 30 (page 54);

- cloning of mannanase and construction of over-expression vectors of mannanase is described in Examples 26-28 (pages 49-51);

- the source and construction of laccase expression vectors is disclosed in Example 32 (pages 56-57).

A person of skill in the art, when reading the Examples as referred to above would readily be able to construct the nucleotide sequences and vectors used and claimed. Applicant therefore respectfully submits that there is no requirement for also providing specific nucleotide sequences in order to satisfy the written description requirement.

While not agreeing to the Examiner's assumptions being made to support the question as to written description, under 35 USC §112, 1st paragraph, Applicant has amended claims 1 and 13 in order to expedite prosecution of the present application. Applicant reserves the right to re-file and prosecute the claims 1 and 13 in their original format should this be desired.

Claims 1 and 13 have been amended to specify that the regulatory region is either a cbh1, cbh2, egl, eg2, eg3, eg5, xln1, or xln2 regulatory region, that the secretion signal is a xylanase secretion signal, and that the genes of interest are selected from the group consisting of mannanases, laccases, endoglucanases, and cellobiohydrolases. It is noted that claims 4-12, 14, 24-29, 32 and 33 depend ultimately from claim1, and claims 15- 23 depend ultimately from claim 13, and these dependant claims include the limitations of claims1 and 13.

Claims 2-3, 30 and 31 have been cancelled without prejudice or disclaimer, thus rendering moot the Examiner's rejection of these claims as to written description support.

Withdrawal of the rejection of claims 1-33 under 35 USC §112 is respectfully requested.

Rejections under 35 U.S.C. § 102

The Examiner has rejected claims 1-30 under 35 USC 102(b), as being anticipated by Suominen et al. The Examiner alleges that Suominen et al teaches a plasmid having a cbh1 promoter, xln1 signal sequence and xln1 coding sequence, and suggests using the plasmid to express other proteins by replacing the coding sequence of the xln1 gene. Applicant respectfully disagrees with Examiner's interpretation of Suominen et al.

Suominen et al. teach an expression construct comprising a cbh1 promoter, a xln2 secretion signal and a xln2 coding sequence (Example 2; page 51, lines 9-13) and an expression construct comprising a cbh1 promoter, a xln1 secretion signal and a xln1 coding sequence (Example 4; page 61, lines 10-13). Both of these constructs comprise a xylanase 2 or 1 secretion signal in combination with their native coding sequence, either xylanase 2 or 1, respectively. Claims1 and 13 are not directed to an expression construct comprising a xylanase secretion signal, combined with a xylanase coding sequence. Therefore, claims 1 and 13, and the claims that depend from claims 1 and 13 are not be anticipated by Suominen et al.

Furthermore, it is submitted that Suominen et al. does not at all suggest the nucleotides sequences defined in independent claims 1 and 13. While Suominen et al. disclose the preparation of a plasmid comprising a cbh1 promoter, a xln1 or a xln 2 secretion signal combined with a xln1 or xly 2 coding sequence, respectively (page 51, lines 9-13; page 61, lines 10-13), there is no teaching or suggestion that the xln1 or xln 2 coding region within this construct may be replaced with another gene encoding a desired enzyme. Rather, Suominen et

al. in reality appear only to teach inserting a gene encoding the desired protein into the cbh1 locus such that it is operably linked to the cbh1 promoter (see page 17, line 21-27 and exemplified on page 46, lines 14-18, the inserted gene encodes the xylanase 2 secretion signal and xylanase 2 coding region, see page 49, lines 17-19) or the pgk promoter (page 18, lines 10-15). It is also stated (page 17, line 28 to page 18, line) that a gene may be inserted into the expression vector, pAMH110, between the cbh1 promoter and terminator. Again, the expression vector pAMH110 does not comprise a signal sequence.

Suominen et al. to the contrary suggest that the coding sequence should retain its own signal sequence, except under certain circumstances. On page 26, lines 12-17 it is indicated that if a desired protein does not posses its own signal sequence, or the signal sequence does not function well in *Trichoderma*, then the coding sequence may be operably linked to a signal sequence homologous or heterologous to *Trichoderma.* However, no specific examples of a desired signal sequence, nor any evidence of the benefit of a specific signal sequence, is provided by Suominen et al.

Independent claims 1 and 13 of the present invention define a nucleotide sequence that comprises a xylanase signal sequence in combination with a mannanase, a laccase, an endoglucanase, or a cellobiohydrolase. The specific examples of the present application provided in the specification demonstrate that the xylanase signal sequence results in enhanced product protein for each of the defined proteins when compared to constructs comprising other signal sequences. For example, reference is made to Examples 12-18 (page 33-41; enhanced β-glycosidase expression), 25, (page 47-49; enhanced endoglucanase expression), 29 (pages 51-53; enhanced mannanase expression), 31 (pages 55-56; enhanced high pH endoglucanase expression), 33 (pages 57-58; enhanced laccase expression), and 38 (pages 61-62; enhanced

xylanase expression). Applicant submits that upon closer examination the Examiner will appreciate that the combination of elements defined in claims 1 and 13 are neither taught nor suggested by Suominen et al.

Claims 4-12, 14, 24-29, 32 and 33 depend ultimately from claim1, and claims 15- 23 depend ultimately from claim 13, and these dependant claims include all limitations of independent claims1 and 13. Claims 2-3, 30 and 31 have been cancelled without prejudice or disclaimer, thus rendering moot Examiner's rejection of these claims as being anticipated.

For the above reasons, Applicant submits that the invention as presently claimed is not anticipated nor is it suggested by Suominen et al. Applicant respectfully requests a withdrawal of Examiner's rejection of claims 1-30 as anticipated, under 35 USC §102.

Favorable reconsideration, withdrawal of the objections and rejections set forth in the last Office Action, and an early Notice of Allowance are requested. The undersigned attorney of record may be reached in our Washington, DC office by telephone at (202) 530-1010. Any additional fee required to render this response timely may be charged to Deposit Acct 06-1205. All correspondence should continue to be directed to our below-listed address.

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APPENDIX: Terminal Disclaimer

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